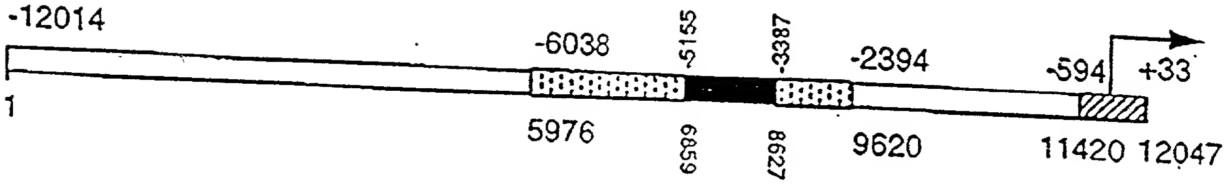

-12014
1
-6038
5976
-5155
6859
-3387
8627
-2394
9620
-594
+33
11420
12047

FIGURE 1

```
HKLK2.LA0   (6998)  AA-CTGAGCCTTGATTATATTG-GAGCTTGGTTGCA-CAG-ACATGTCGA
                    :: :: :: : ::: :::: :: : :::      :  ::: :::  :: :
PSE         ( 509)  AATCT-AG-C-TGA-TATAGTGTG-GCTCAAAACCTTCAGCACAAATC-A

HKLK2.LA0   (7044)  CCACCTTCATGGCTGAACTTTAGTACTTAGCCCCTCCAGACGTCTACAGC
                     :::: : : : ::  : : : ::   : :   : ::: ::  :: :::
PSE         ( 553)  -CACCGTTA-GACT--A-TCTGGT--GT-G--GC-CCAAAC--CTTCAGG

HKLK2.LA0   (7094)  TGATAGGCTGTAACCCAACAT-TGTCACCATAAATCACATTGTTAGACTA
                    ::: :    :  :: : : :: :: ::  :: : :: ::     :: : :
PSE         ( 590)  TGA-ACAAAGGGACTCTA-ATCTGGCAGGAT-ATTC-CA----AAG-C-A

HKLK2.LA0   (7143)  TCCAGTG-TGGCC-CAAGCTCCCGTGTAAACACAGGCACTCTAAACAG--
                    :  :: : :: :: :  ::    :   ::: : : : :    ::: ::
PSE         ( 630)  T-TAGAGATGACCTCTTGC-AAAG-AAAAAGAAATGGAAAAGAAAAAGAA

HKLK2.LA0   (7189)  -G-CAGGATATTTCAAAAGCTT-AGAGATGACCTCCCAGGAGCTGAATGC
                     :  :::: :    ::::     :::::::::::: ::::  ::::  :
PSE         ( 677)  AGAAAGGAAAAAAAAAAAAAAAAAGAGATGACCTCTCAGGCTCTGAGGGG

HKLK2.LA0   (7236)  AAA-GACCTGGCCTCTTTGGGCAAGGAGAATCCTTTACCGCACACTCTCC
                    ::: : ::::   :::::: ::::::  : :::: :   ::::: :::::
PSE         ( 727)  AAACG-CCTGAGGTCTTTGAGCAAGGTCAGTCCTCTGTTGCACAGTCTCC

HKLK2.LA0   (7285)  TTCACAGGGTTATTGTGAGGATCAAATGTGGTCATGTGTGTGAGACACCA
                     ::::::::: ::::::: ::::::::::::::: :::: :::: :::::
PSE         ( 776)  CTCACAGGGTCATTGTGACGATCAAATGTGGTCACGTGTATGAGGCACCA
                                    :                    :::

HKLK2.LA0   (7335)  GCACATGTCTGGCTGTGGAGAGTGACTTCTA--TGTGTGCTAACATTGCT
                    ::::::: :::::: ::: ::::: : : ::  ::: ::::  :: ::::
PSE         ( 826)  GCACATGCCTGGCTCTGGGGAGTGCCGTGTAAGTGTATGCTTGCACTGCT
                    :: : :     :    ::  :      :::  : : : :          :

HKLK2.LA0   (7383)  GAGTGCTAAGAAAGTATTAGGCATGGCT-TTCAGCACTCACAGATGCTCA
                    :: ::::  : : :: : ::: ::   : ::::::::: :::::::::::
PSE         ( 876)  GAATGCTTGGGATGTGTCAGGGAT-TATCTTCAGCACTTACAGATGCTCA
                            ::    :           :      :     :   ::
```

FIGURE 2A

```
HKLK2.LA0     ( 7432)   TCTAATCCTCACAACATGGCTACAGGG-TGGGCACTACTAGCCTCATTTG
                        ::: ::::::::: :::  :::  ::: :::: : :::: ::::::::::
PSE           (  925)   TCTCATCCTCACAGCATCACTA-TGGGATGGGTATTACTGGCCTCATTTG
                        :  ::     : ::  :        :::     :  : :::     : :

HKLK2.LA0     ( 7481)   ACAGAGGAAAG-GACTGTGGATAAGAAGGGGGTGACCAATAGGTCAGAGT
                        :  :: ::::: : :::::: : :::: :::: ::::: :::  ::: :
PSE           (  974)   ATGGA-GAAAGTGGCTGTGGCTCAGAAAGGGGGGACCACTAGACCAGGGA
                                :  : : :        :   :        :    :

HKLK2.LA0     ( 7530)   CATTCTGGATGCAAGGGG-CTCCAGAGGACCATGATTAGACATTGTCTGC
                        :: :::::::::  :::: ::::::: ::::::::  :  ::    ::::
PSE           ( 1023)   CACTCTGGATGC-TGGGGACTCCAGA-GACCATGACCACTCACCAACTGC
                              :  :            :    :    ::   ::      :

HKLK2.LA0     ( 7579)   AGAGAAATT----ATGG-CTGGATGTCTCTGCCCCGGAAAGGG-GGA--T
                        :::::::::     ::: :: :::::: ::: :: ::: :::: :::  :
PSE           ( 1071)   AGAGAAATTAATTGTGGCCT-GATGTCCCTGTCCTGGAGAGGGTGGAGGT
                              :: :     :   :  :: :      :  :     ::    ::

HKLK2.LA0     ( 7621)   GCACTTTCCTTGACCCCCTATCTCAGATCTTGACTTTGAG-GTTATCTCA
                        : :: :::  : ::: :::: ::  :: : :  :::: :: : : : ::
PSE           ( 1120)   GGACCTTCACTAACCTCCTACCT-TGACCCTCTCTTTTAGGGCTCTTTCT
                        :  :    :  :   :        :: :      : :            :

HKLK2.LA0     ( 7670)   GACTTCCTCTATGATACCAGGAGCCCATCATAATCTCTCTGTGTCCTCTC
                        ::: ::: : ::: ::: :::: :::  :::  : : :::::  :: ::
PSE           ( 1169)   GACCTCCACCATGGTACTAGGA-CCC--CATTGTAT-TCTGT-ACC-CT-
                        ::     :  :                 ::  ::    : :  : :

HKLK2.LA0     ( 7720)   CCCTTCCTCAGTCTTACTG-CCCACTCTTCCCAGCTCCATCTCCAGCTGG
                          : :  : : :: :: :: ::: : :: :::: :: ::  :::::::
PSE           ( 1212)   --C-T--TGACTC-TA-TGACCCCCACTGCCCA-CTGCA--TCCAGCT--
                            :    :        :  :     :         ::        :

HKLK2.LA0     ( 7769)   CCAGGTGTAGCCACAGTACCTAACTCT-TTGCAGAGAACTATAAATGTGT
                           :: ::  :: :  : :::: :::: :: :  ::  ::    : :::
PSE           ( 1250)   ---GG-GT--CC-C-CT-CCTATCTCTATT-CCCAG--CTGGCCA-GTGC
                           :               :        ::                 :

HKLK2.LA0     ( 7818)   A-TCCTACAGGGGAGAAAAAAA-AAAAG-AACTCTGAAAGAGCTGACATT
                        : : :: ::: :   :          :: ::::::::: : :::::::::
PSE           ( 1287)   AGT-CT-CAGTGCCCACCT~~GT~~TTGTCAGTAACTCTGAAGGGGCTGACATT
                            :  :        :   ::  ::     :                :

HKLK2.LA0     ( 7865)   TTACCGACTTGCAAACACATAAGCTAACCTGCCAG--TTTTGT----GCT
                        :::: :::::::::::: :::::::::: : ::::  ::::::    :::
PSE           ( 1335)   TTACTGACTTGCAAACAAATAAGCTAACTTTCCAGAGTTTTGTGAATGCT
                        :  :  :  :: :  :          ::        : :   :  : : :

HKLK2.LA0     ( 7909)   GGTAGAACT-CATGAGACTCCTGGGTCAGAGGCAAAAGATTTTATTACCC
                        :: :: : : ::::::::::::: :::::::::::: : ::::: : : :
PSE           ( 1385)   GGCAG-AGTCCATGAGACTCCTGAGTCAGAGGCAAAGGCTTTTACTGCTC
                        :             :::      :::   ::
```

FIGURE 2B

```
HKLK2.LA0       (7958)  ACAGCTAAGGAGGCAGCATGAACTTTGTGTTCACATTTGTTCACTTTGCC
                        :::::: :: :: ::::::::  ::  :::::::::: :: ::: :::::
PSE             (1434)  ACAGCTTAGCAGACAGCATGAGGTTCATGTTCACATTAGTACACCTTGCC
                        .:         :  ::   :  :: ::   ::               : :

HKLK2.LA0       (8008)  CCCC--AATTCATAT-GGGATGATCAGAGCAGTTC-AGGTGGATG--G-A
                        ::::  :: :: : : ::: ::: :::::::: :: :::::::::  :
PSE             (1484)  CCCCCCAAATCTTGTAGGG-TGACCAGAGCAG-TCTAGGTGGATGCTGTG
                        :      :  ::    : :    :  :    :  :   ::    :

HKLK2.LA0       (8051)  CA-CAGGGGTTTGTGGCAAAGGTGAGCAACCTAG-GCTTAGAAATCCTCA
                        ::  ::::::::::: ::  :::::: ::::: : : :::: ::::::::
PSE             (1532)  CAGAAGGGGTTTGTGCCACTGGTGAGAAACCT-GAGATTAGGAATCCTCA
                         :        : : ::  :::: :      :   ::        :   :

HKLK2.LA0       (8099)  ATCTTATAAGAAGGTACT---AGCAAACTTGTC-CAGTCTTTGTATCTGA
                        ::::::: :   :: ::     :::::: :: : ::: :::::: :::::
PSE             (1581)  ATCTTAT-ACTGGG-ACAACTTGCAAACCTG-CTCAGCCTTTGTCTCTGA
                           : :      :  ::    :   ::        :   ::: : : :

HKLK2.LA0       (8145)  CGGAGATATTATCTTTATAAT-TGGG-TTGAAAGCAGACCTACTCTGGAG
                         : :::::::::::: :: :: : :: :::::: ::::::::::::::::
PSE             (1628)  TGAAGATATTATCTTCATGATCTTGGATTGAAAACAGACCTACTCTGGAG
                        :    : :      :: :: : :     :       : : :   ::   :

HKLK2.LA0       (8193)  GAACATATTGTATTTATTGTCCT-GAACAGTAAACAAATCTGCTGTAAAA
                        :::::::::::::  :::::::: : :::::::::::::::: :::  ::
PSE             (1678)  GAACATATTGTATCGATTGTCCTTG-ACAGTAAACAAATCTGTTGT--AA
                        :     : ::   :   :  : : :    : :::    :  : :

HKLK2.LA0       (8242)  TAGACGTTAACTTTATTATCTAAGG-CAGTAAGCAAACCTAGATCTGAAG
                         :::: ::: ::::::::::: ::: :::::::::: ::: :::::: ::
PSE             (1725)  GAGACATTATCTTTATTATCT-AGGACAGTAAGCAAGCCTGGATCTG-AG
                                :

HKLK2.LA0       (8291)  -GCGATACCATCTTGCAAGGCTATCTGCTGTACAAATATGCTTGAAAAGA
                         : :::: :::::::::::: :  ::::: :::::: :: :::::::  :
PSE             (1773)  AGAGATATCATCTTGCAAGGATGCCTGCTTTACAAACATCCTTGAAACAA

HKLK2.LA0       (8340)  TGGTCCAGAAAAGAAAACGGTATTATTGCCTTTGCTCAGAAGACACACAG
                           ::::::::: :::: ::: ::  :: :::::::::::::::::::::
PSE             (1823)  CAATCCAGAAAA-AAAAAGGTGTTGCTGTCTTTGCTCAGAAGACACACAG

HKLK2.LA0       (8390)  AAACATAAGAGAACCATGGAAAATTGTCTCCCAACACTGTTCACCCAGAG
                        : :: : : ::::::::::: ::::: :::::::: ::::::: ::::::
PSE             (1872)  ATACGTGACAGAACCATGGAGAATTGCCTCCCAACGCTGTTCAGCCAGAG

HKLK2.LA0       (8440)  CCTTCCACTCTTGTCTGCAGGACAGTCTTAACATCCCATCATTAG-T-GT
                        :::::::: ::::::::::::::::::: ::: : ::: :::::  :  :
PSE             (1922)  CCTTCCACCCTTGTCTGCAGGACAGTCTCAACGTTCCACCATTAAATACT
                                  :: :::                     : :: ::    ::
```

FIGURE 2C

```
HKLK2.LA0     (8488)    --GTCTACCACATCTGGCTTCACCGTGCCTAACCAAGATTTCTAGGTCCA
                           :::: ::::::  :::::    ::::::::::::  ::::::::::
PSE           (1972)    TCTTCTATCACATCCTGCTTCTTTATGCCTAACCAAG-GTTCTAGGTCCC
                              :        ::    : :   :      : :   :: :::   :

HKLK2.LA0     (8536)    GTTCCCCACCATGTTTGGCAGTGCCCCACTGCCAACCCCAGAATAAGGGA
                        : :  : ::  ::: ::::::  : :::::::::: :::::::::::: :
PSE           (2021)    GAT--CGACTGTGTCTGGCAGCACTCCACTGCCAAACCCAGAATAAGGCA
                              ::   :   :: :   :      ::              :   :

HKLK2.LA0     (8586)    GTGCTCAGAATTCCGA
                        : :::::: :: ::::
PSE           (2069)    GCGCTCAGGATCCCGA
                        :            : :
```

FIGURE 2D

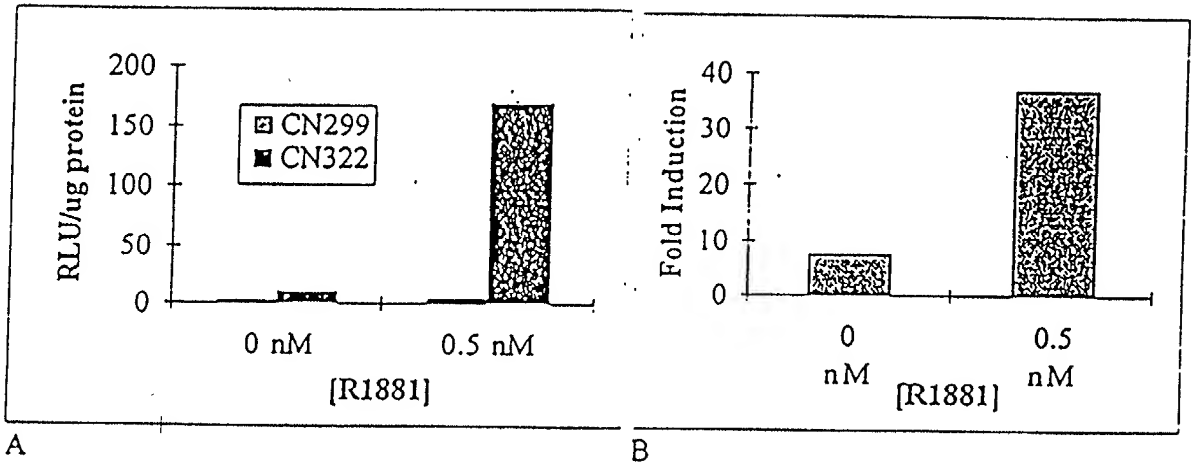

RLU/ug protein
200
150
100
50
0
☐ CN299
■ CN322
0 nM
0.5 nM
[R1881]
A
Fold Induction
40
30
20
10
0
0 nM
0.5 nM
[R1881]
B

FIGURE 3

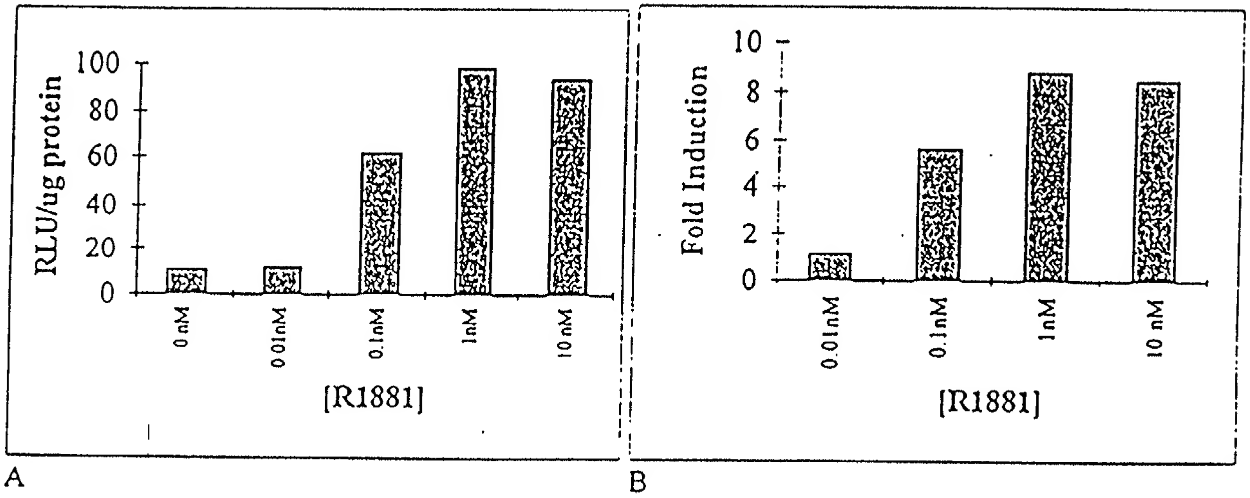

RLU/ug protein
100
80
60
40
20
0
0 nM
0.01nM
0.1nM
1nM
10 nM
[R1881]
A
Fold Induction
10
8
6
4
2
0
0.01nM
0.1nM
1nM
10 nM
[R1881]
B

FIGURE 4

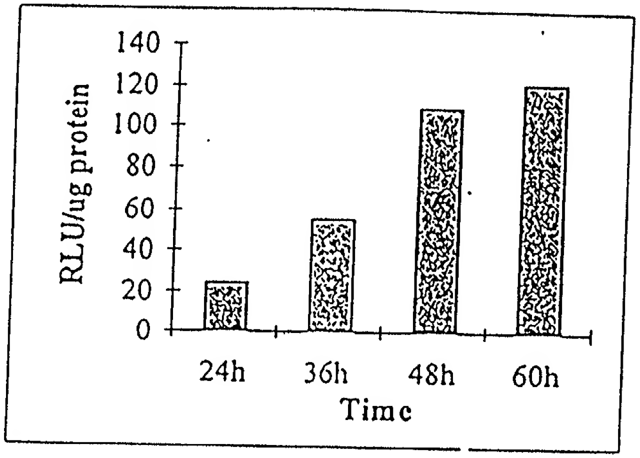


FIGURE 5

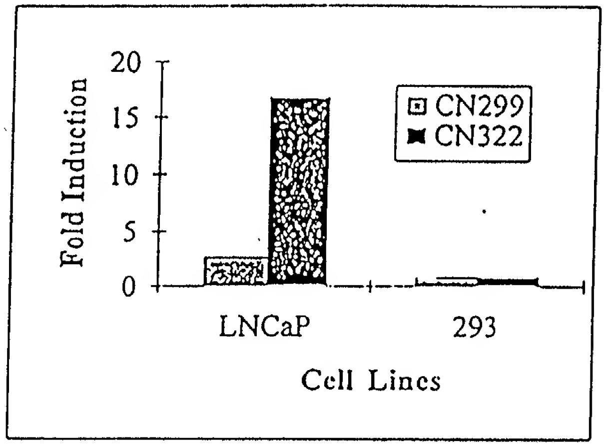


FIGURE 6

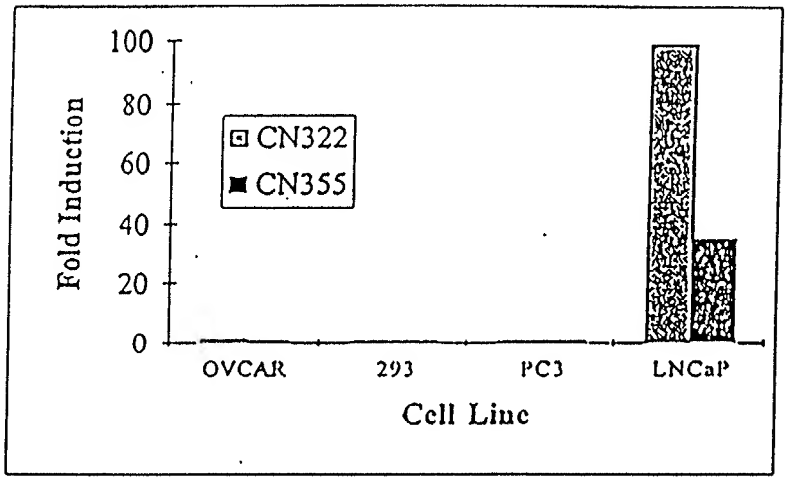
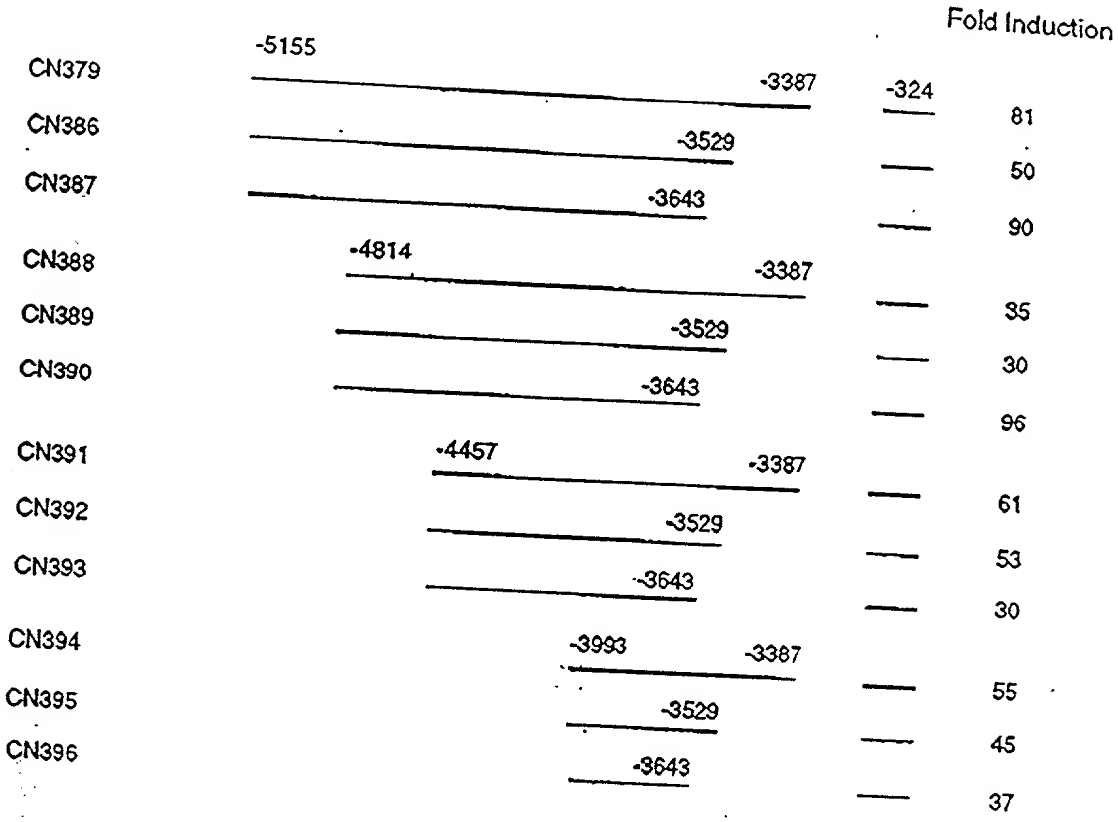

Fold Induction
100
80
60
40
20
0
CN322
CN355
OVCAR
293
PC3
LNCaP
Cell Line

FIGURE 7



Fold Induction
CN379
-5155
-3387
-324
81
CN386
-3529
50
CN387
-3643
90
CN388
-4814
-3387
35
CN389
-3529
30
CN390
-3643
96
CN391
-4457
-3387
61
CN392
-3529
53
CN393
-3643
30
CN394
-3993
-3387
55
CN395
-3529
45
CN396
-3643
37

FIGURE 8

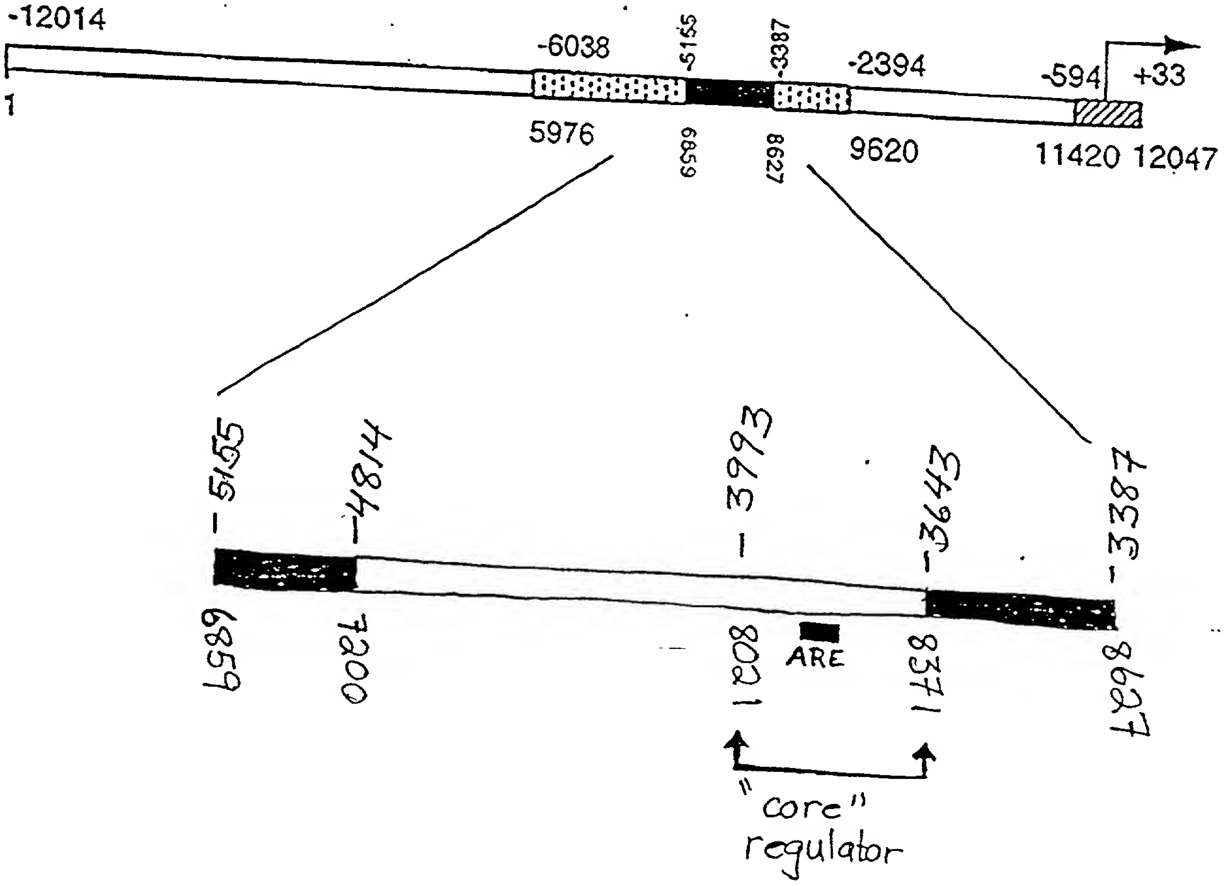

-12014
1
-6038
5976
-5155
6859
-3387
8627
-2394
9620
-594
11420
+33
12047
-5155
6859
-4814
7200
-3993
8021
ARE
-3643
8371
-3387
8627
"core" regulator

FIGURE 9

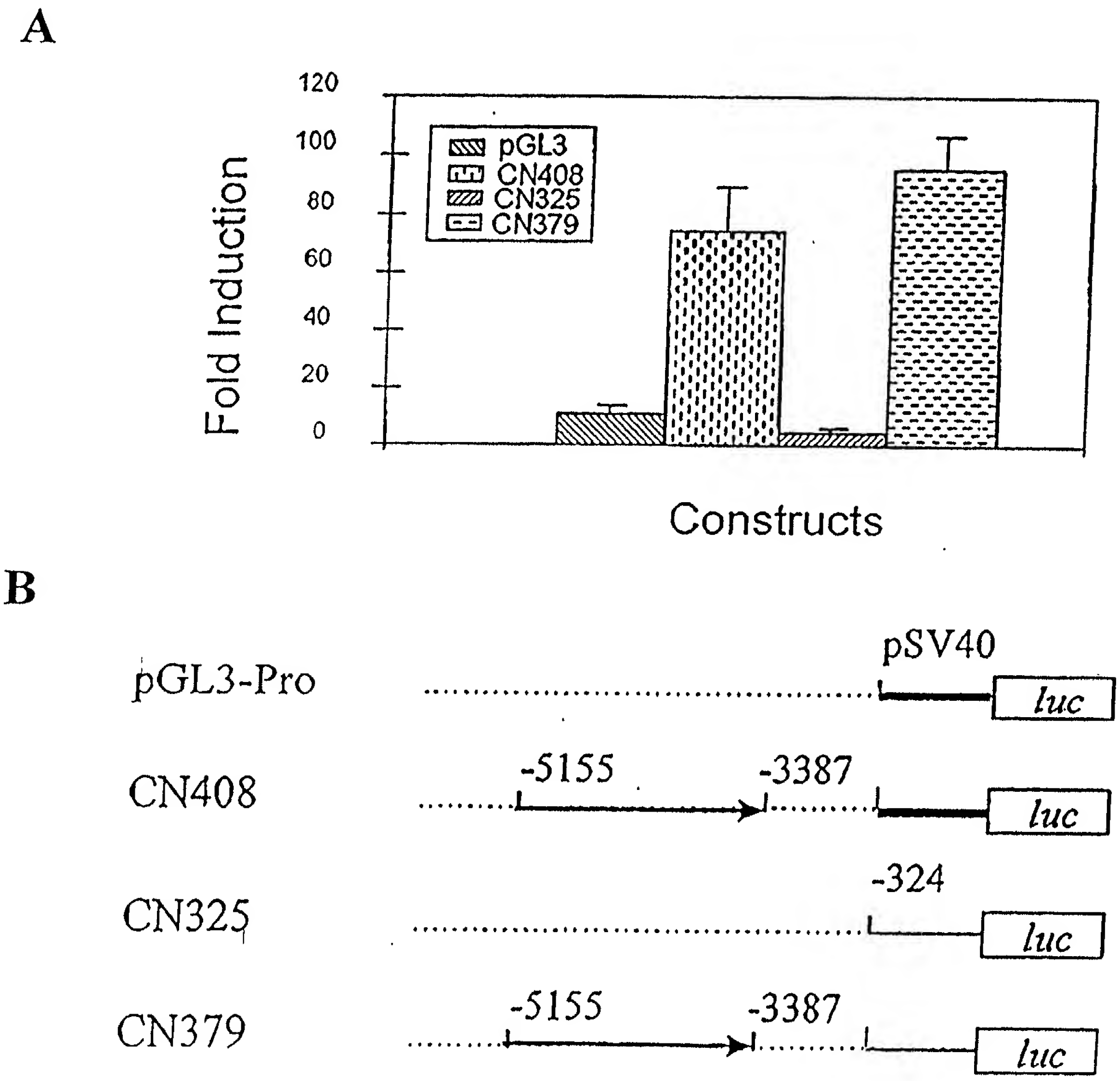

A
Fold Induction
120
100
80
60
40
20
0
pGL3
CN408
CN325
CN379
Constructs
B
pGL3-Pro
pSV40
luc
CN408
-5155
-3387
luc
CN325
-324
luc
CN379
-5155
-3387
luc

FIGURE 10

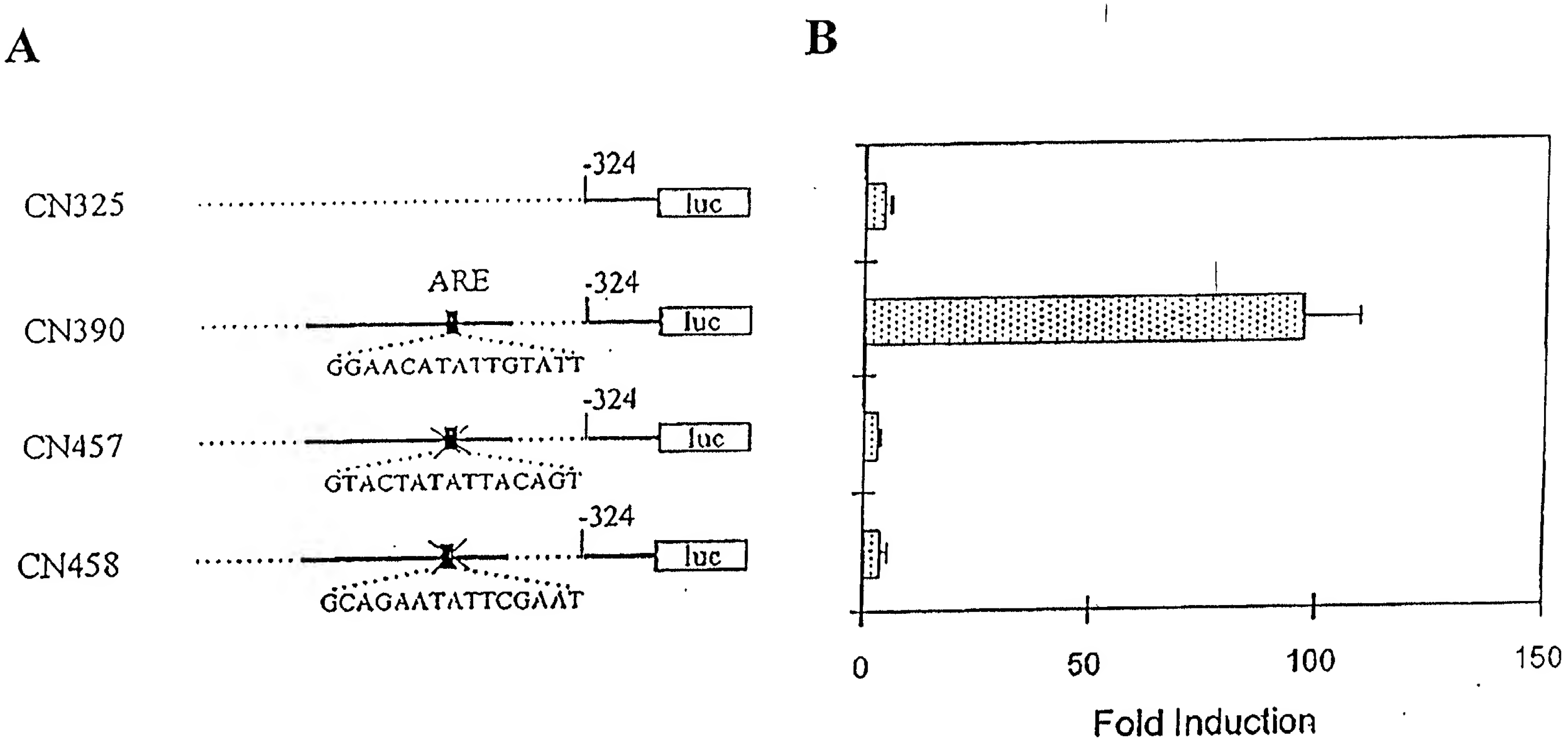

A
B
CN325
CN390
CN457
CN458
-324
ARE
luc
GGAACATATTGTATT
GTACTATATTACAGT
GCAGAATATTCGAAT
0
50
100
150
Fold Induction

FIGURE 11

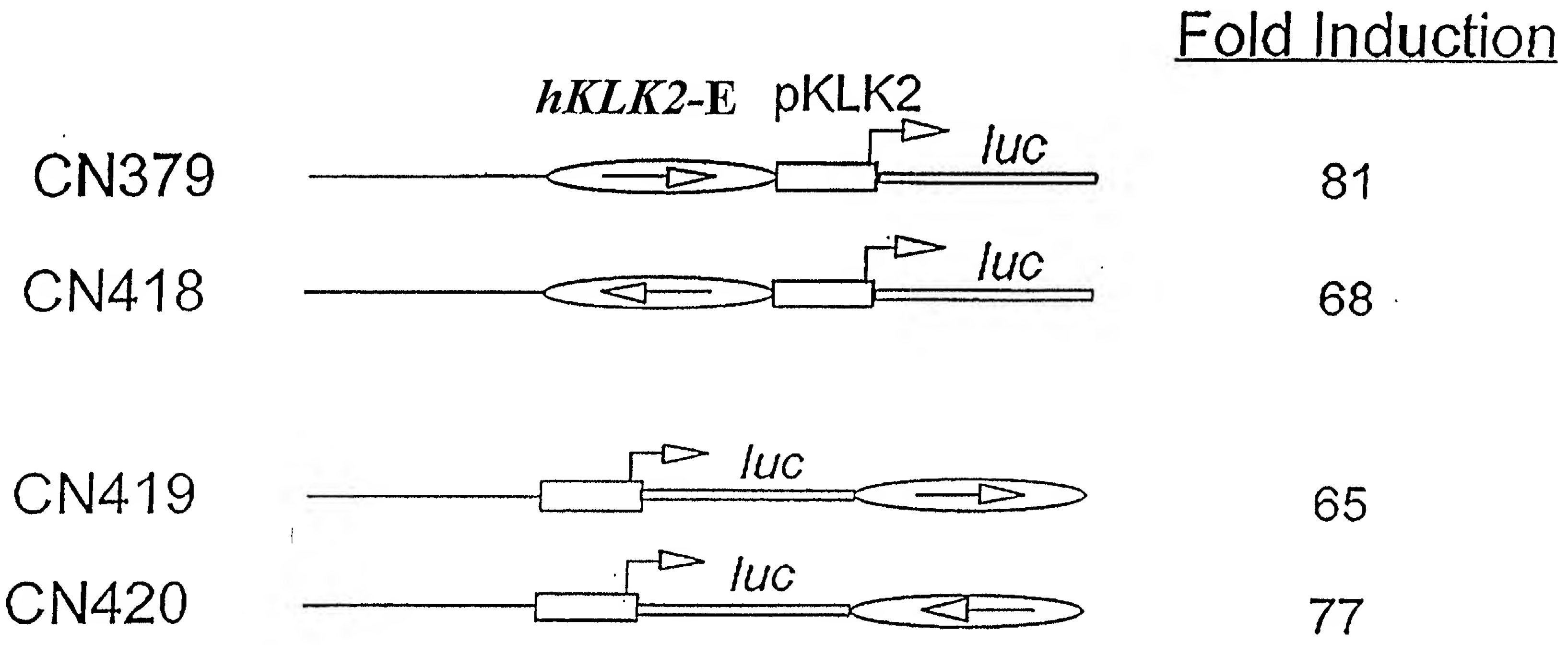

Fold Induction
hKLK2-E
pKLK2
luc
CN379
81
luc
CN418
68
luc
CN419
65
luc
CN420
77

FIGURE 12

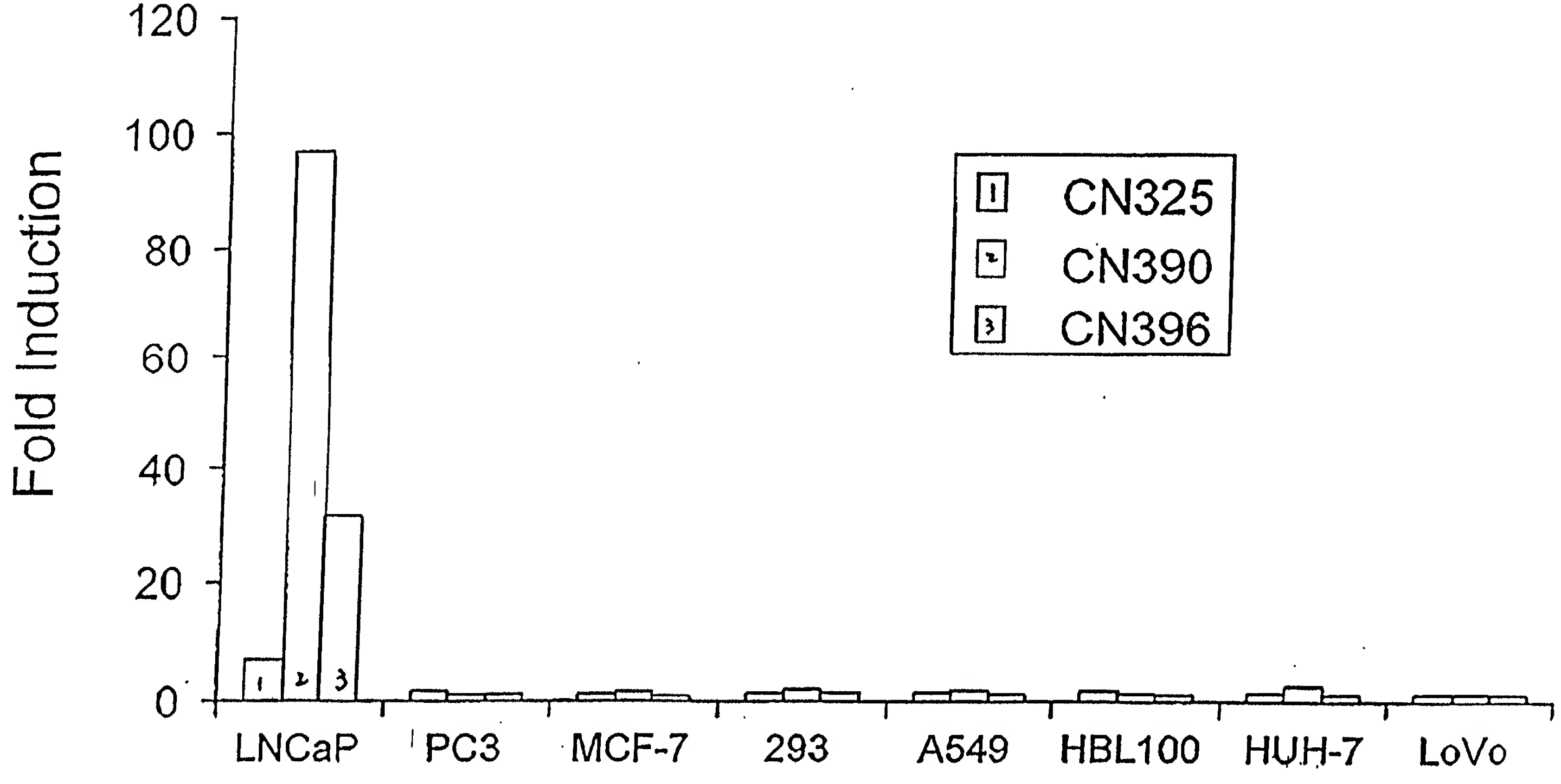

Fold Induction
120
100
80
60
40
20
0
1
2
3
LNCaP
PC3
MCF-7
293
A549
HBL100
HUH-7
LoVo
Cell Line
1 CN325
2 CN390
3 CN396

FIGURE 13

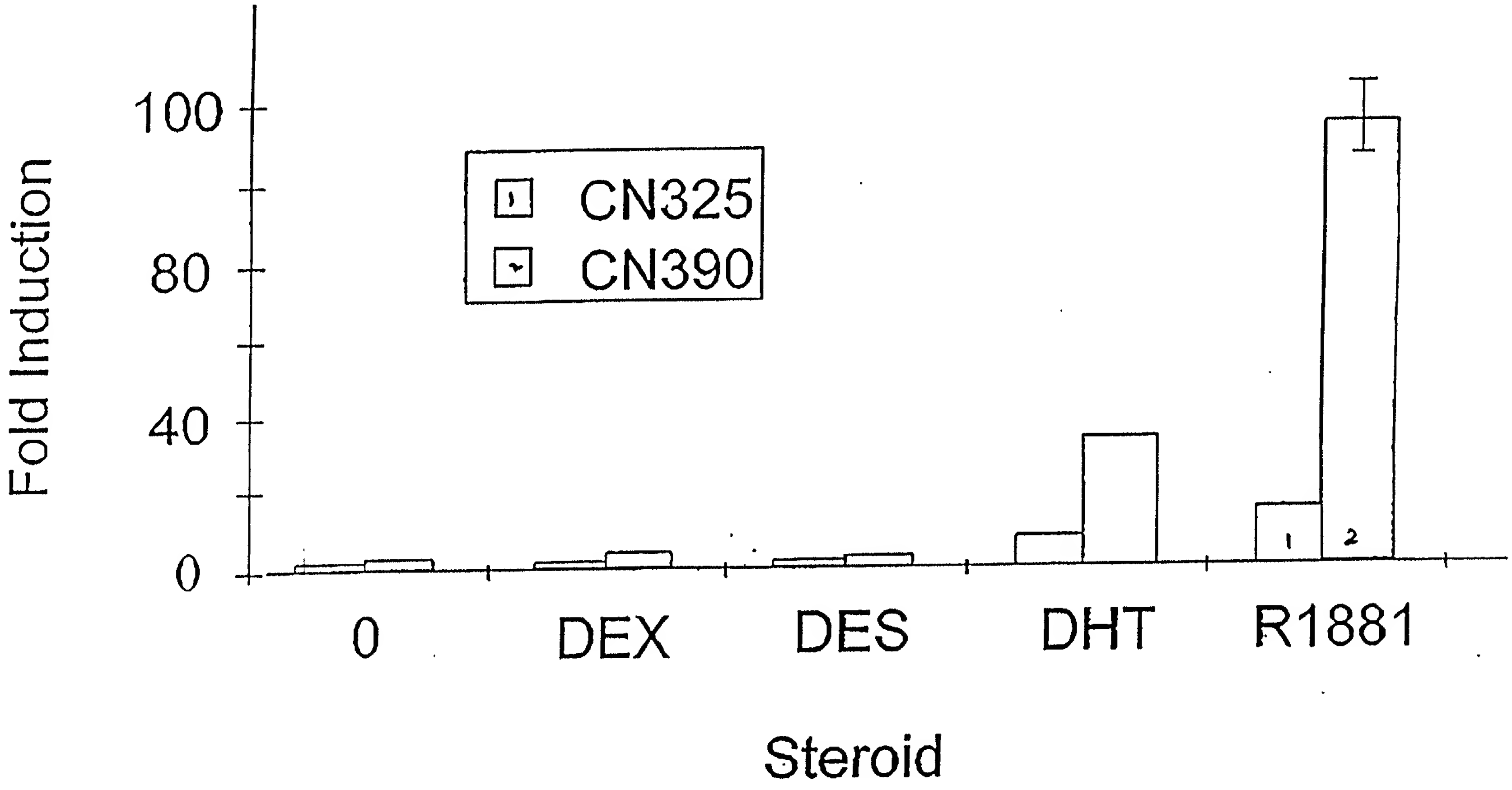

Fold Induction
100
80
40
0
CN325
CN390
1
2
0
DEX
DES
DHT
R1881
Steroid

FIGURE 14

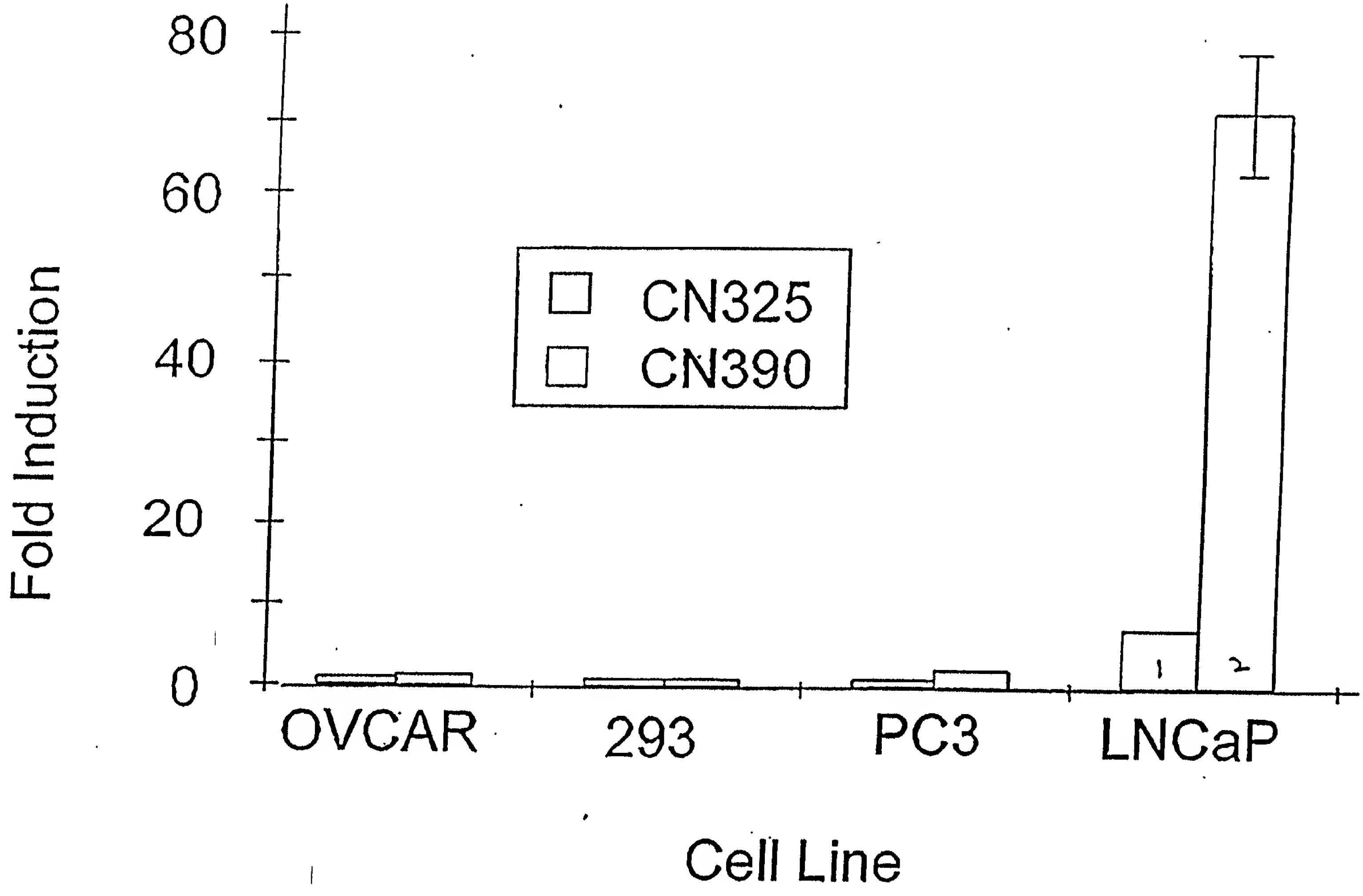

80
60
40
20
0
Fold Induction
CN325
CN390
1
2
OVCAR
293
PC3
LNCaP
Cell Line

FIGURE 15

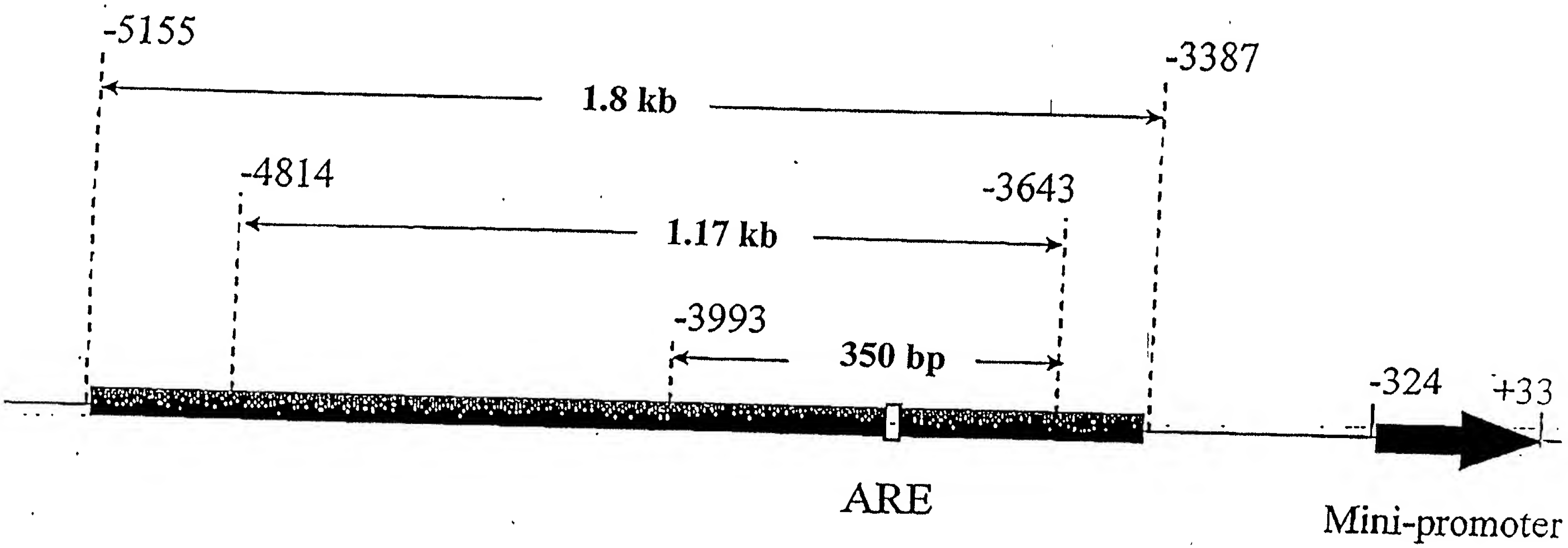

-5155
1.8 kb
-3387
-4814
1.17 kb
-3643
-3993
350 bp
-324
+33
ARE
Mini-promoter

FIGURE 16

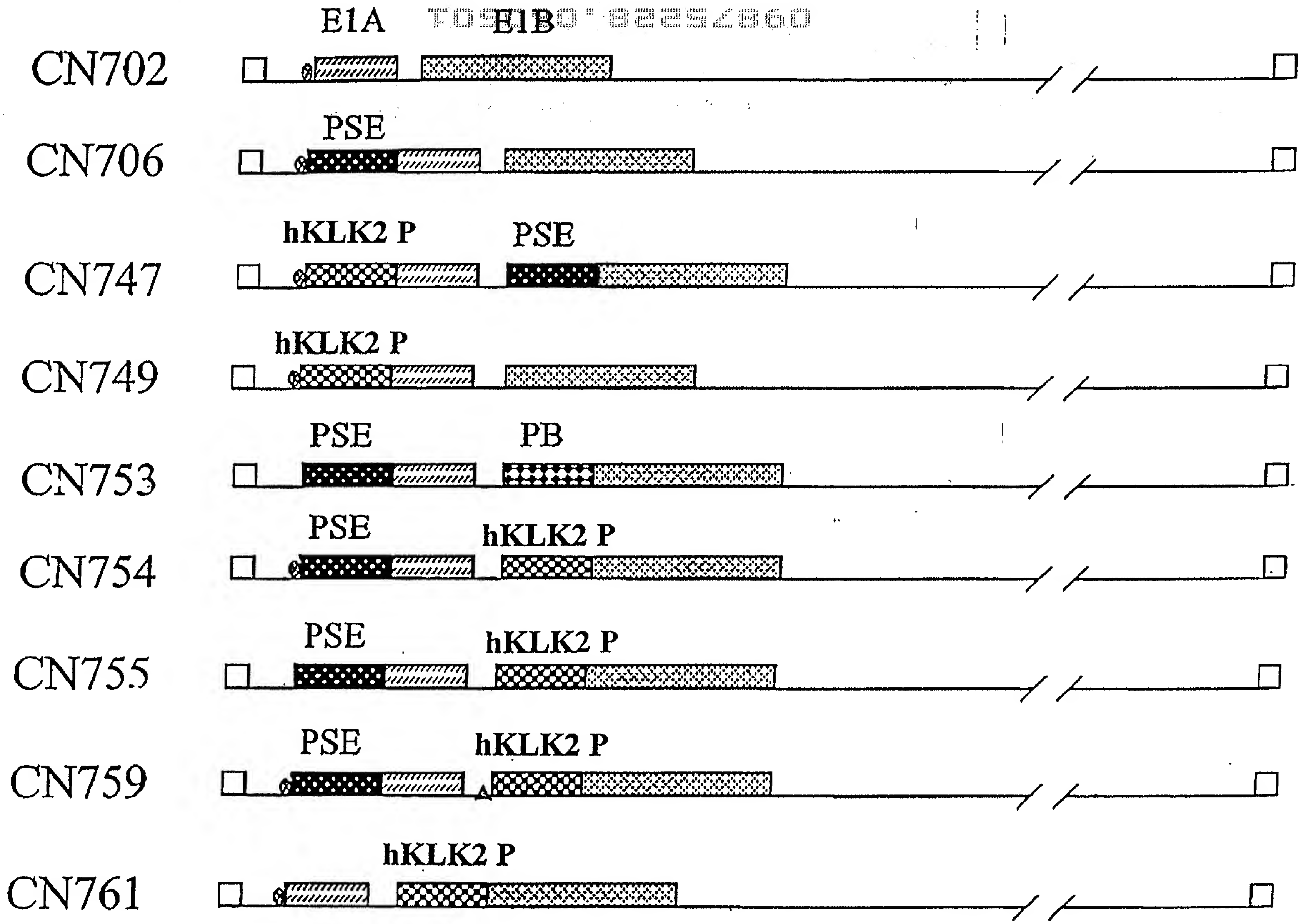

E1A
E1B
CN702
PSE
CN706
hKLK2 P
PSE
CN747
hKLK2 P
CN749
PSE
PB
CN753
PSE
hKLK2 P
CN754
PSE
hKLK2 P
CN755
PSE
hKLK2 P
CN759
hKLK2 P
CN761

FIGURE 17A

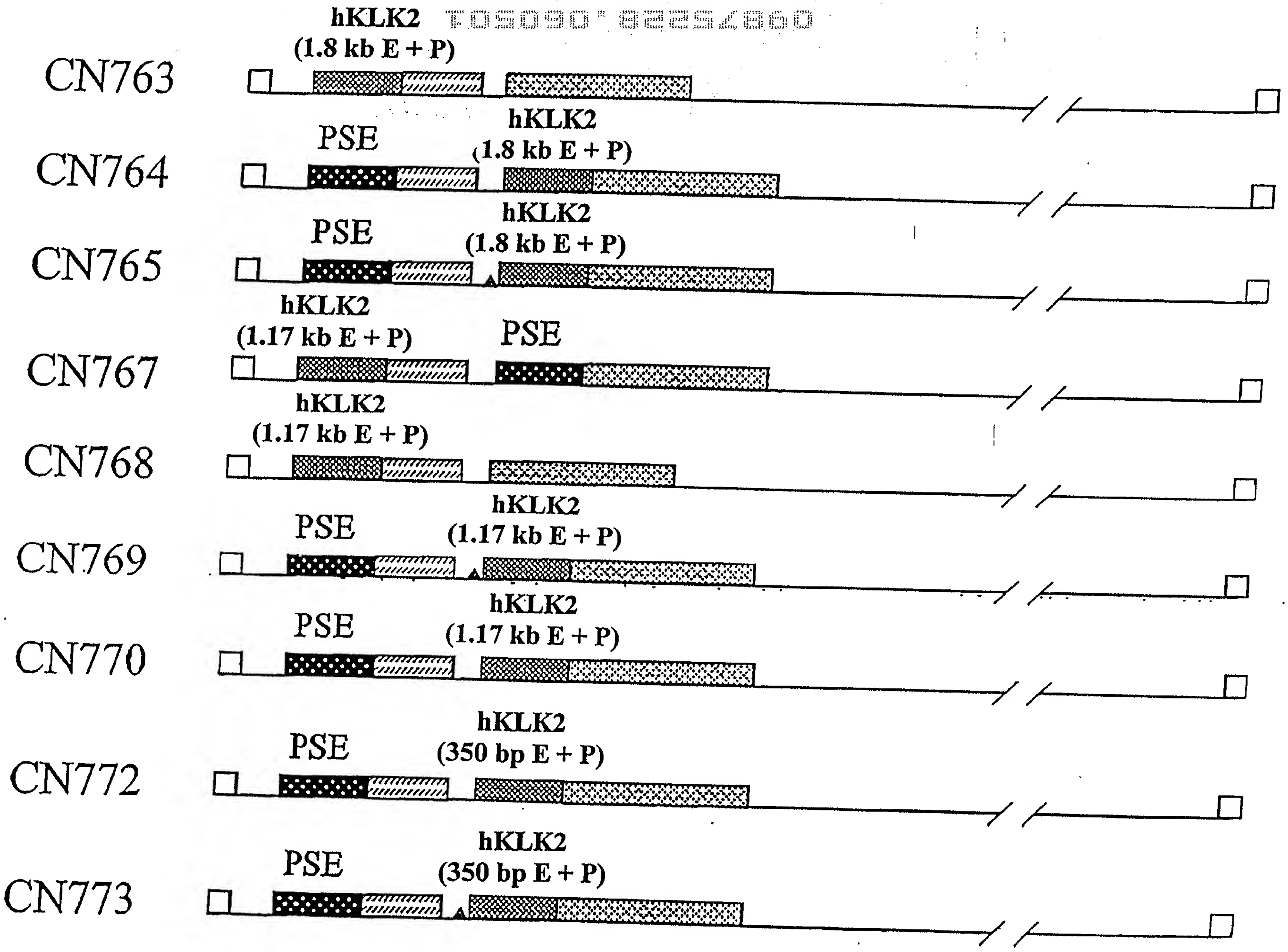

CN763
hKLK2
(1.8 kb E + P)
CN764
PSE
hKLK2
(1.8 kb E + P)
CN765
PSE
hKLK2
(1.8 kb E + P)
CN767
hKLK2
(1.17 kb E + P)
PSE
CN768
hKLK2
(1.17 kb E + P)
CN769
PSE
hKLK2
(1.17 kb E + P)
CN770
PSE
hKLK2
(1.17 kb E + P)
CN772
PSE
hKLK2
(350 bp E + P)
CN773
PSE
hKLK2
(350 bp E + P)

FIGURE 17B

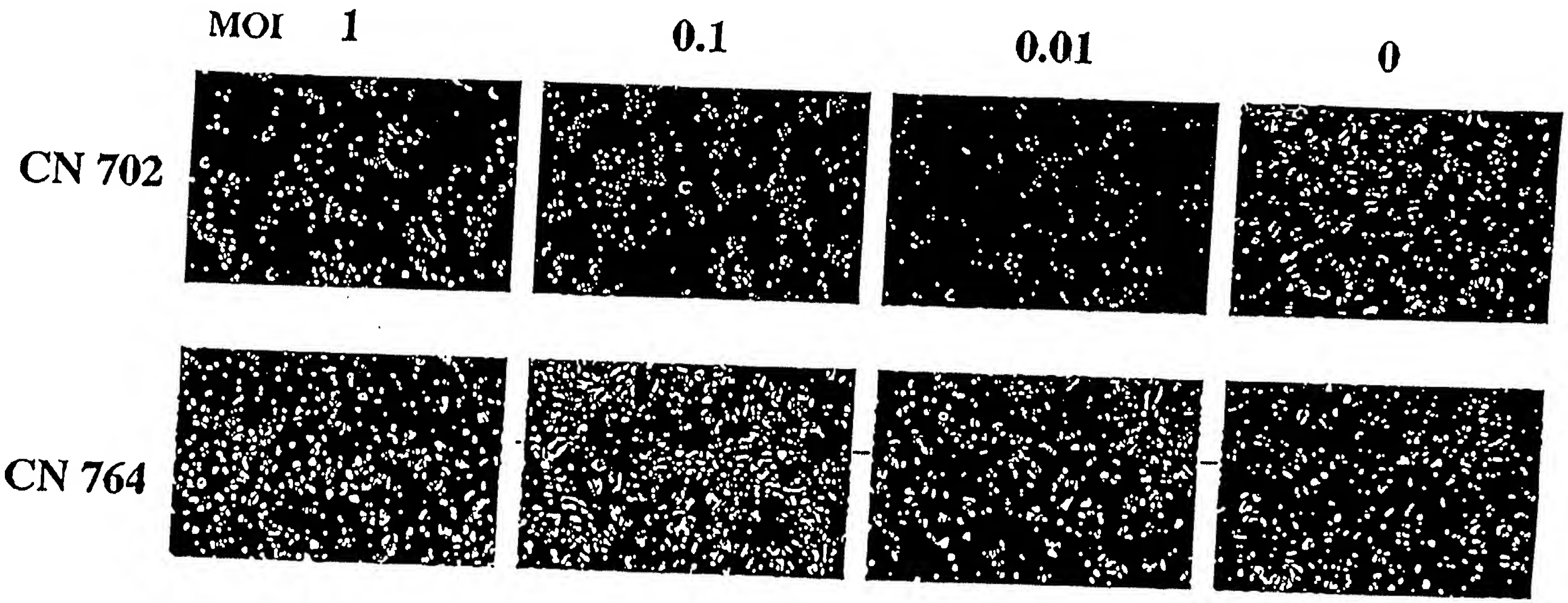


FIGURE 18

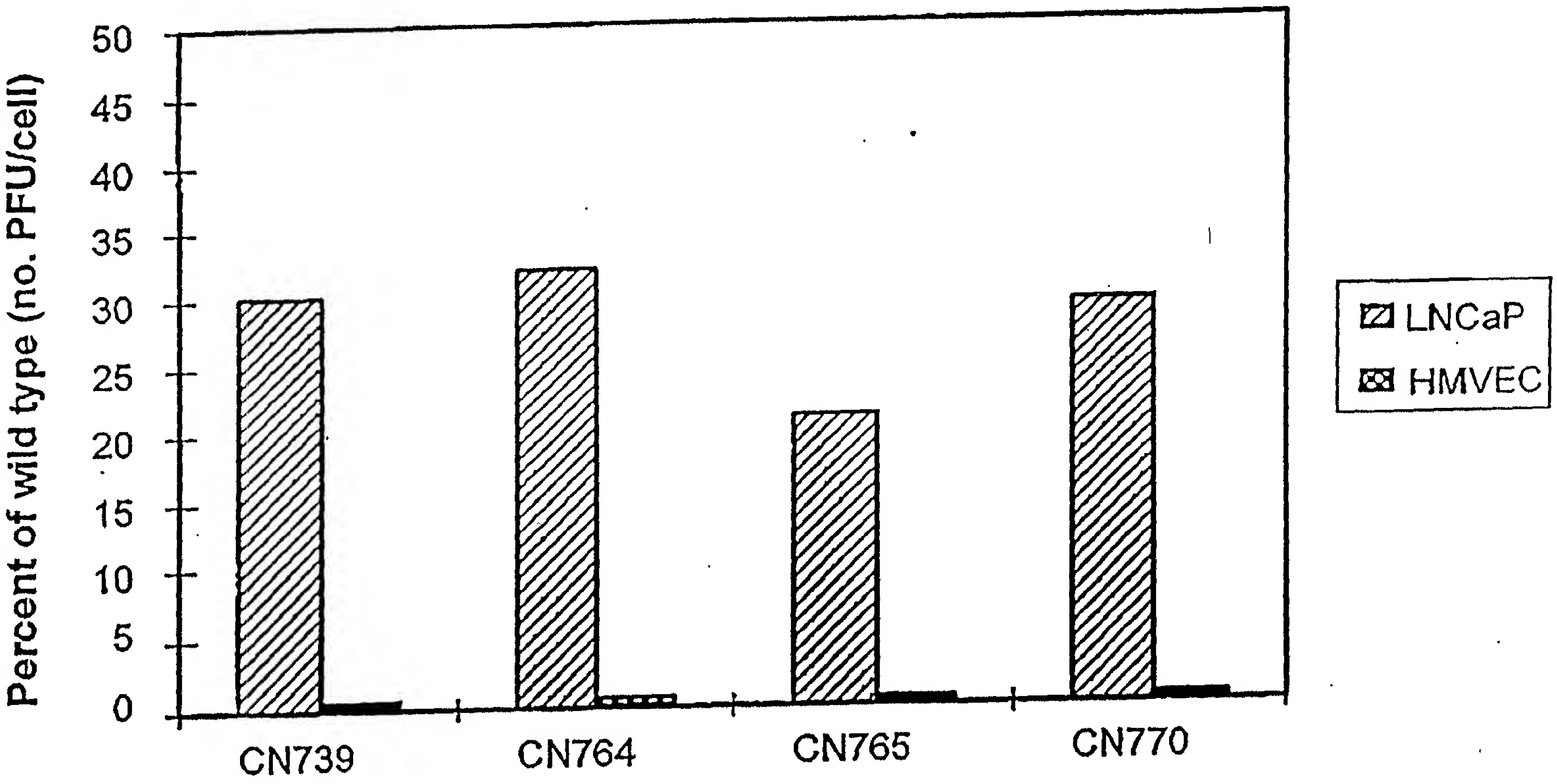

Percent of wild type (no. PFU/cell)
50
45
40
35
30
25
20
15
10
5
0
CN739
CN764
CN765
CN770
▨ LNCaP
▩ HMVEC

FIGURE 19

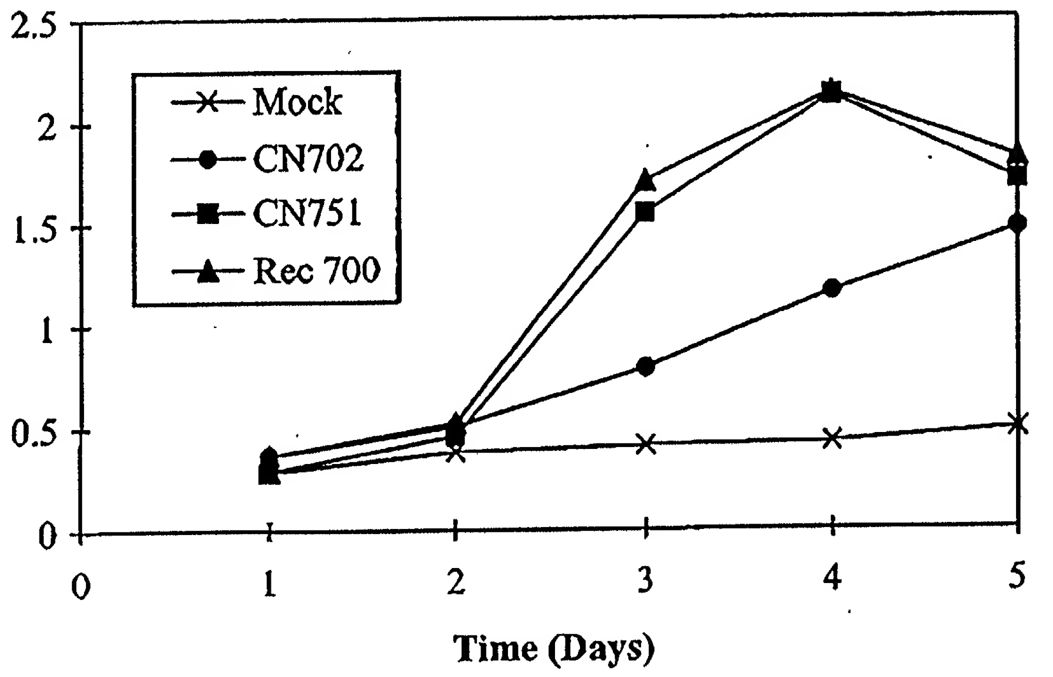


FIGURE 20

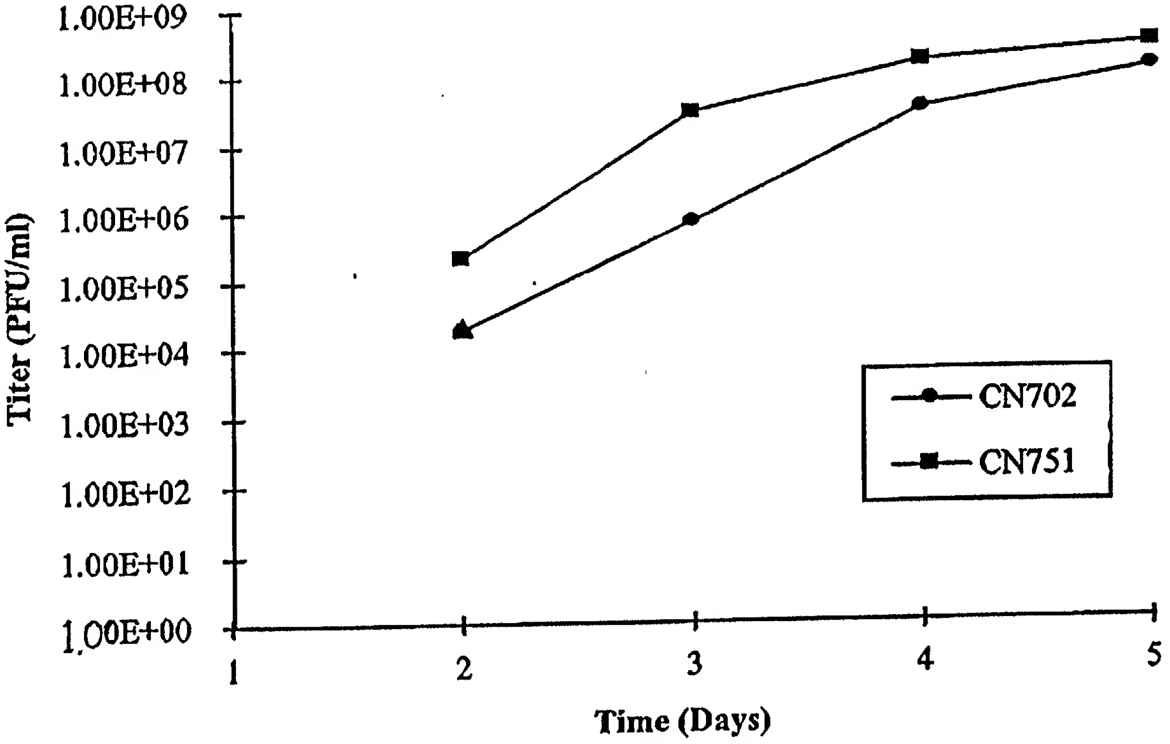

Titer (PFU/ml)
1.00E+09
1.00E+08
1.00E+07
1.00E+06
1.00E+05
1.00E+04
1.00E+03
1.00E+02
1.00E+01
1.00E+00
1
2
3
4
5
Time (Days)
CN702
CN751

FIGURE 21

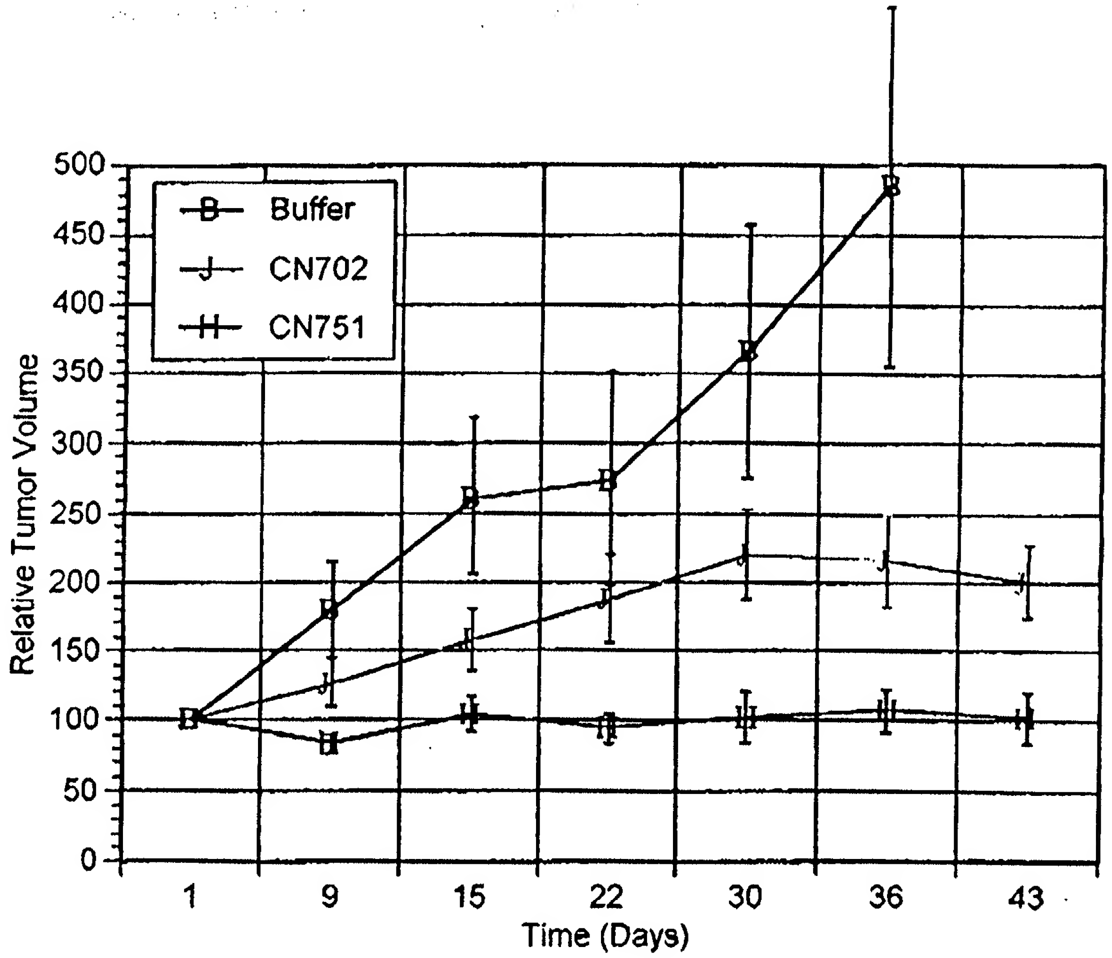

500
450
400
350
300
250
200
150
100
50
0
Relative Tumor Volume
B Buffer
J CN702
H CN751
1
9
15
22
30
36
43
Time (Days)

FIGURE 22

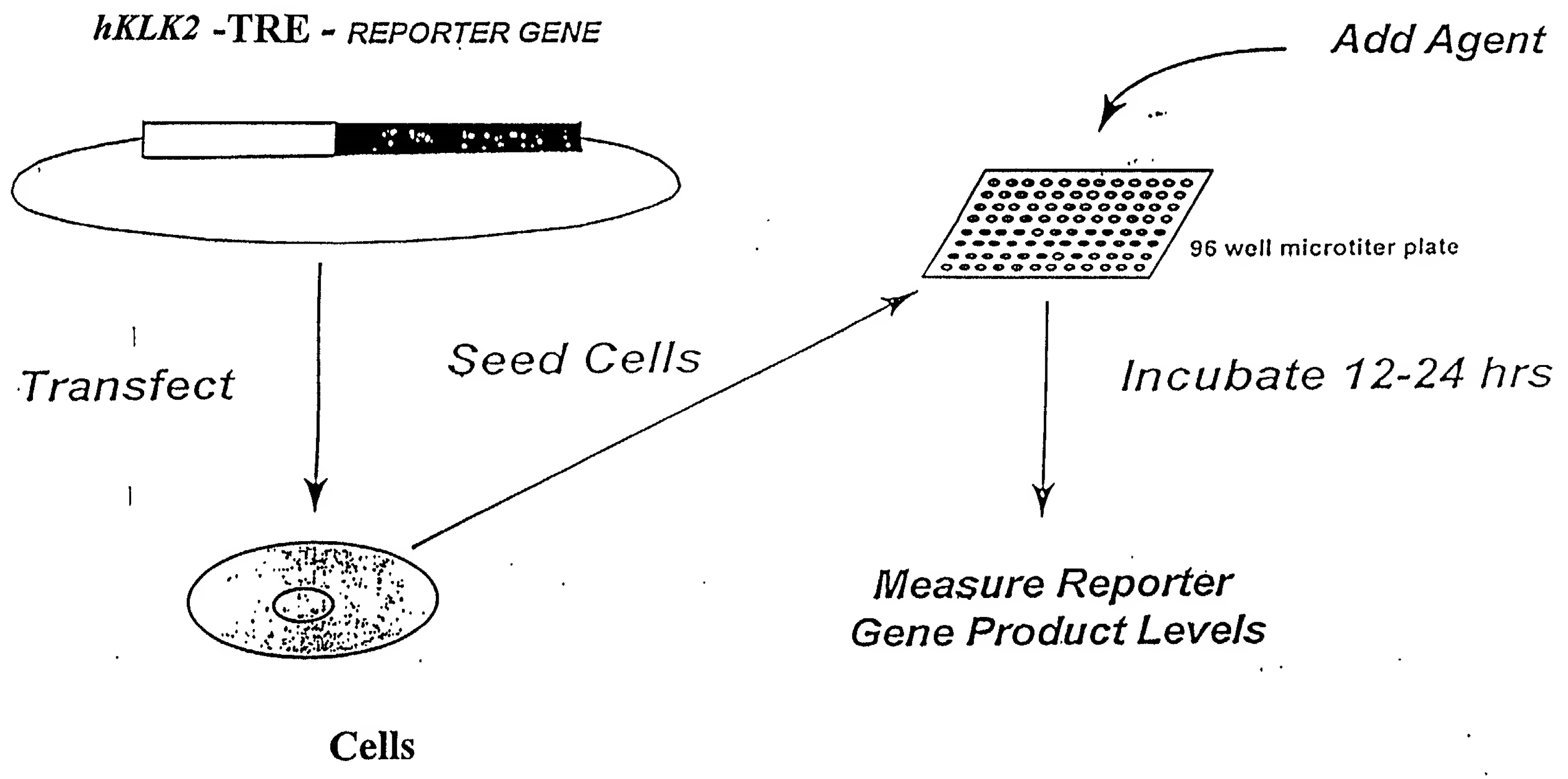

hKLK2 -TRE - *REPORTER GENE*
Add Agent
96 well microtiter plate
Transfect
Seed Cells
Incubate 12-24 hrs
Measure Reporter Gene Product Levels
Cells

FIGURE 23A

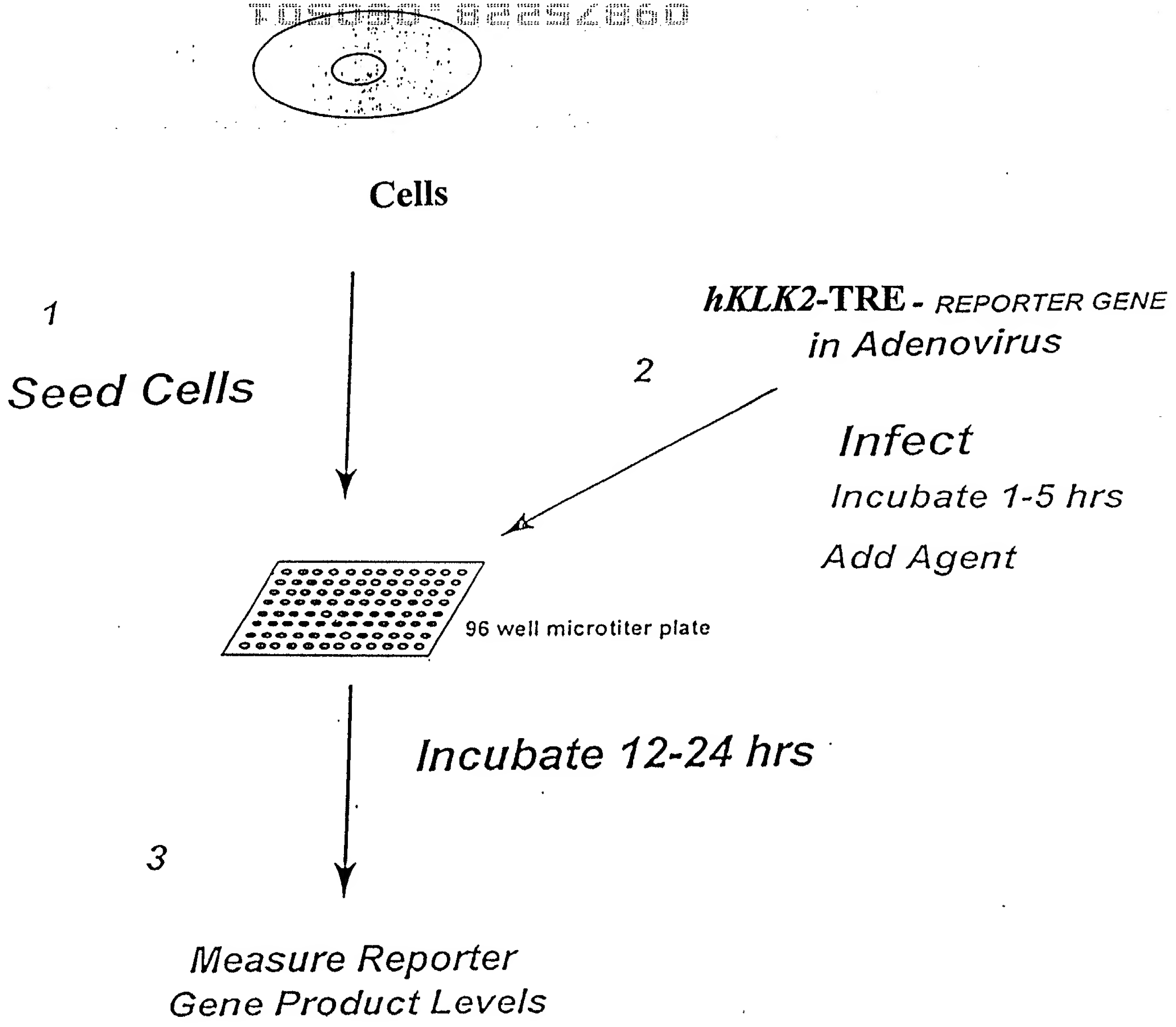

Cells
1
Seed Cells
2
hKLK2-TRE - REPORTER GENE
in Adenovirus
Infect
Incubate 1-5 hrs
Add Agent
96 well microtiter plate
Incubate 12-24 hrs
3
Measure Reporter
Gene Product Levels

FIGURE 23B

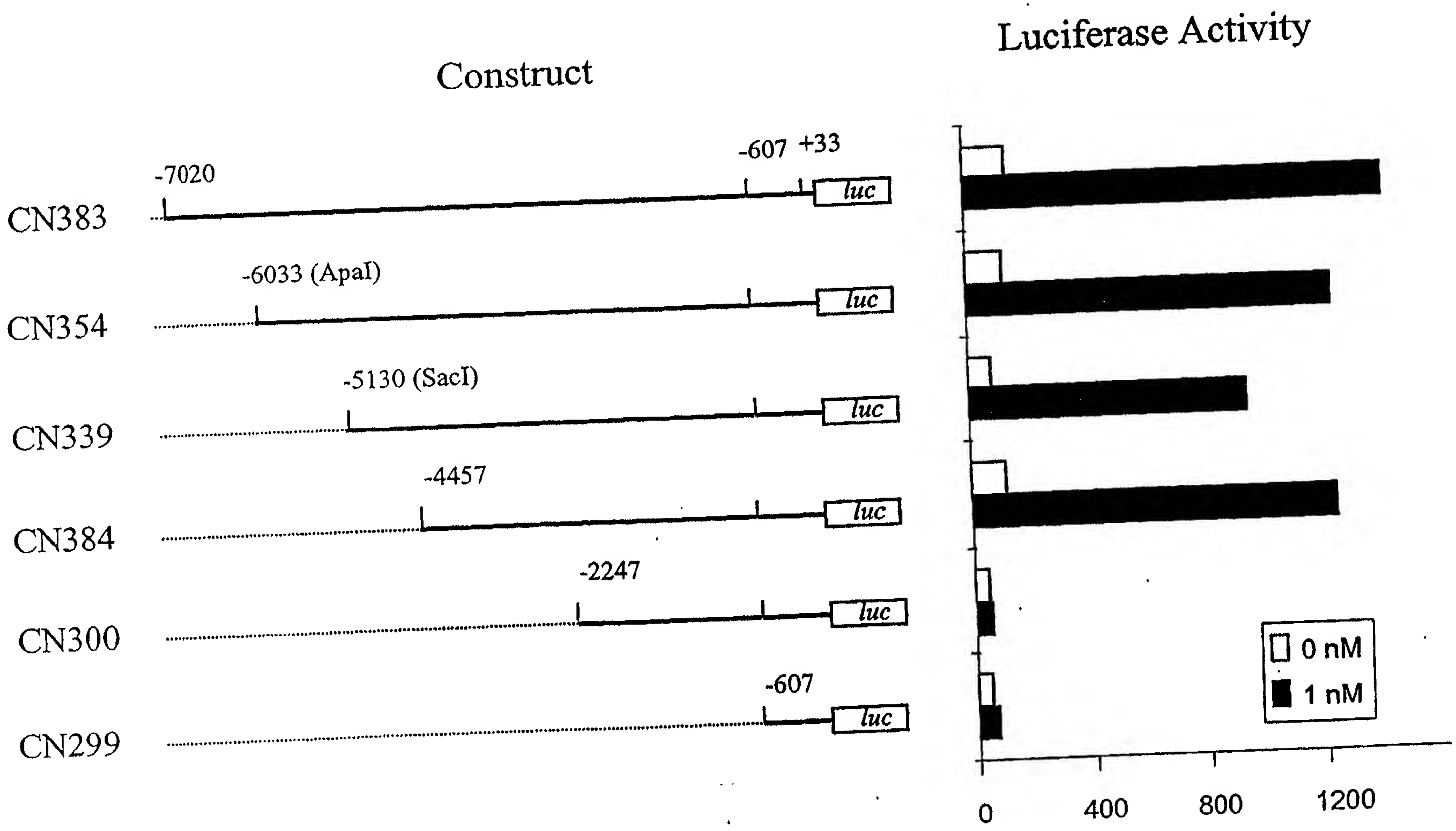

Construct
Luciferase Activity
CN383
CN354
CN339
CN384
CN300
CN299
-7020
-607
+33
-6033 (ApaI)
-5130 (SacI)
-4457
-2247
-607
luc
0 nM
1 nM
0
400
800
1200

FIGURE 24A

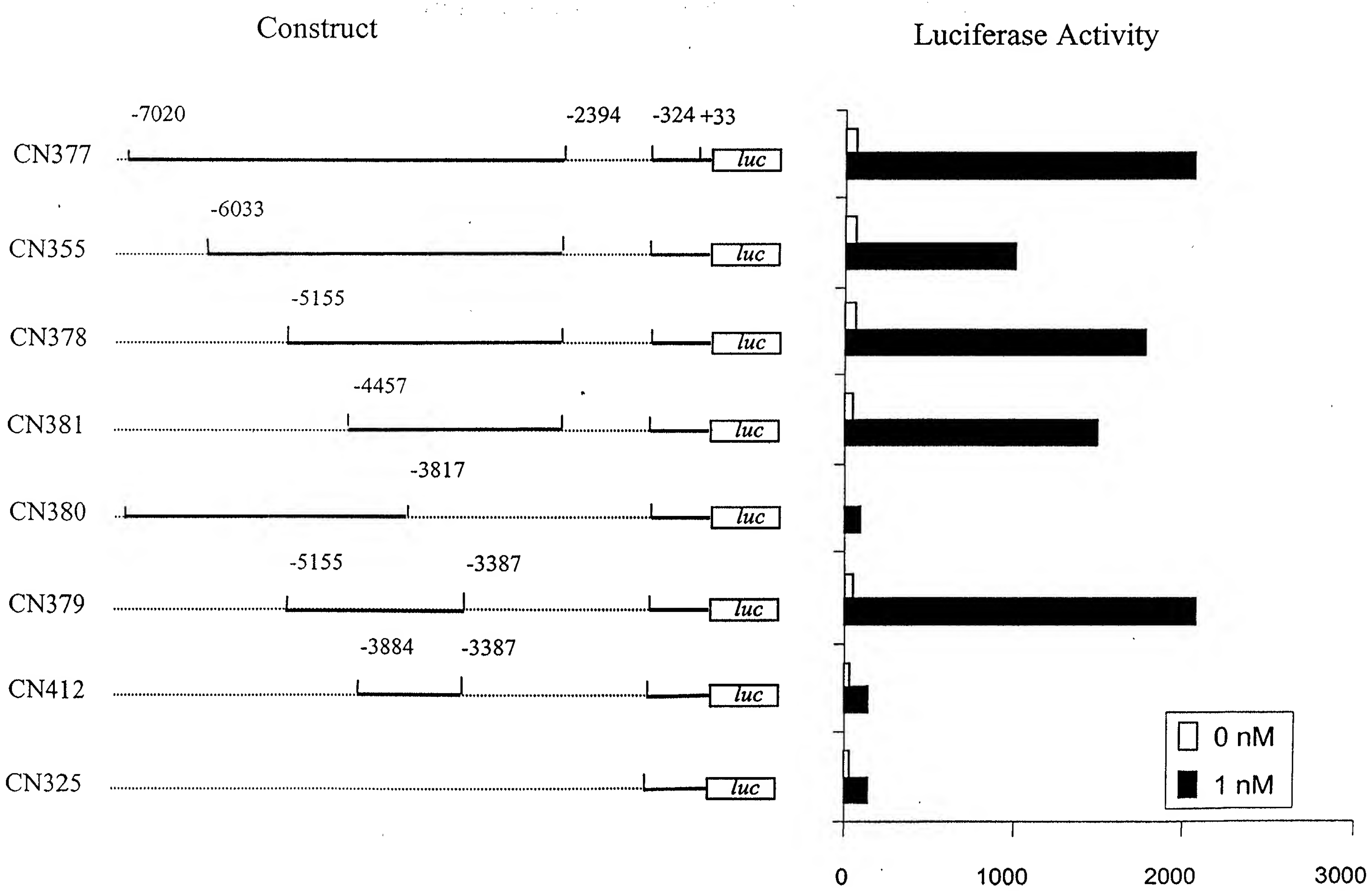

Construct
Luciferase Activity
-7020
-2394
-324 +33
CN377
luc
-6033
CN355
-5155
CN378
-4457
CN381
-3817
CN380
-5155
-3387
CN379
-3884
-3387
CN412
CN325
0 nM
1 nM
0
1000
2000
3000

FIGURE 24B

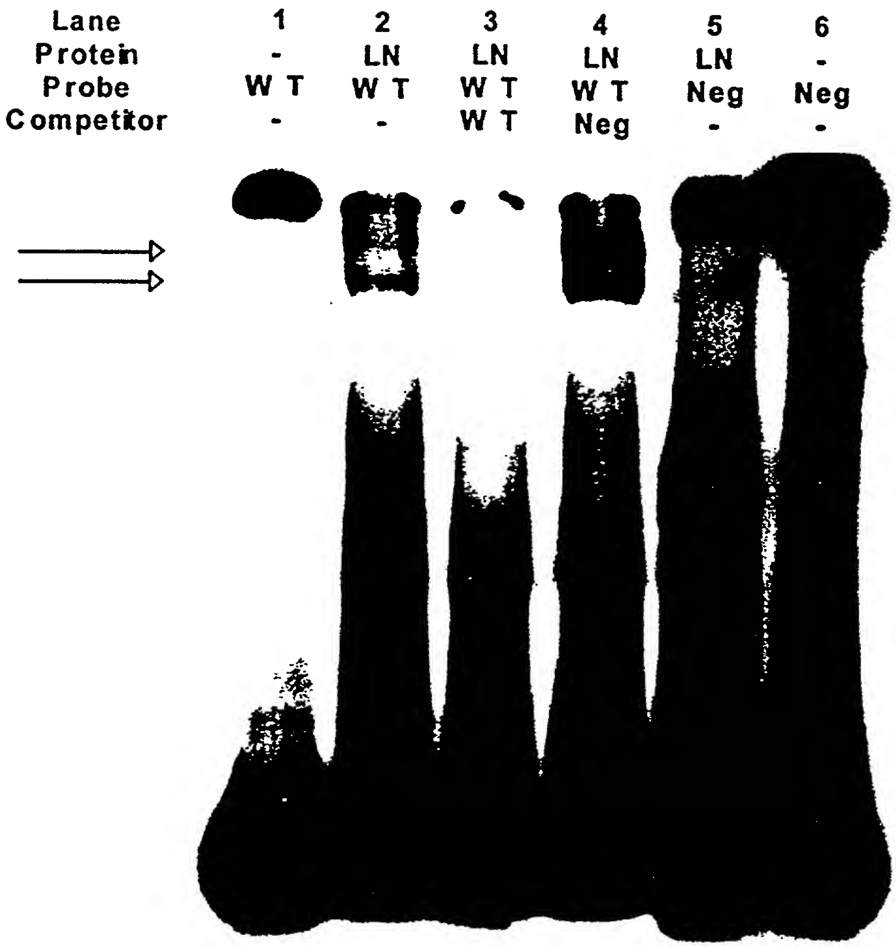

Lane
Protein
Probe
Competitor
1
-
W T
-
2
LN
W T
-
3
LN
W T
W T
4
LN
W T
Neg
5
LN
Neg
-
6
-
Neg
-

FIGURE 25A

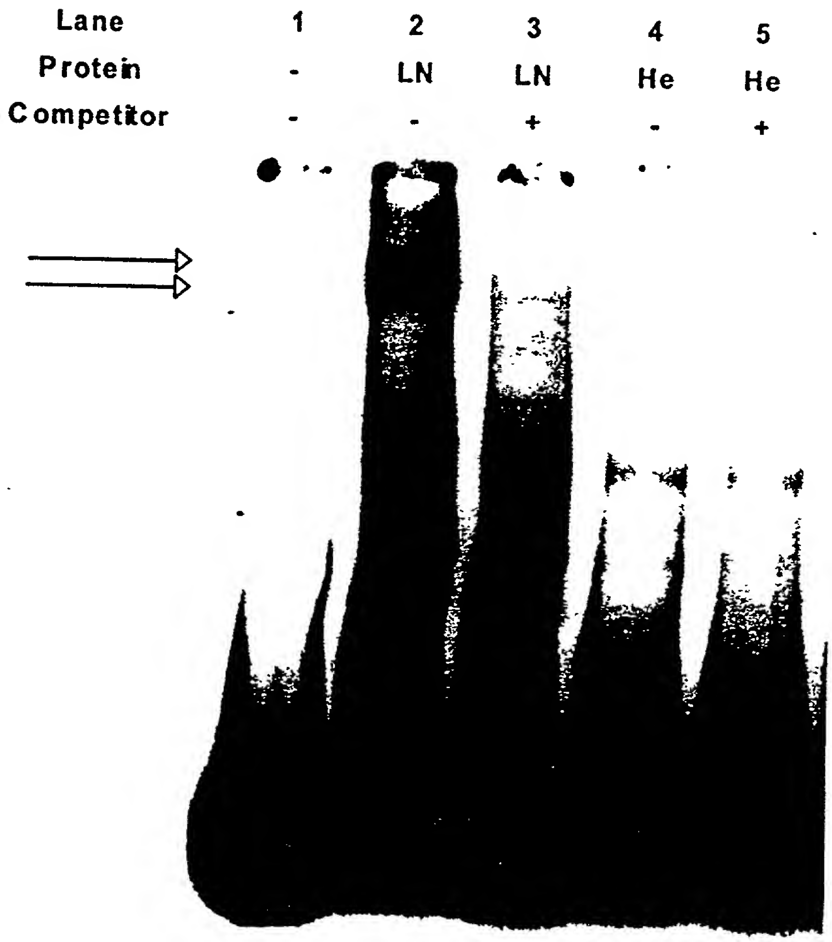


FIGURE 25B

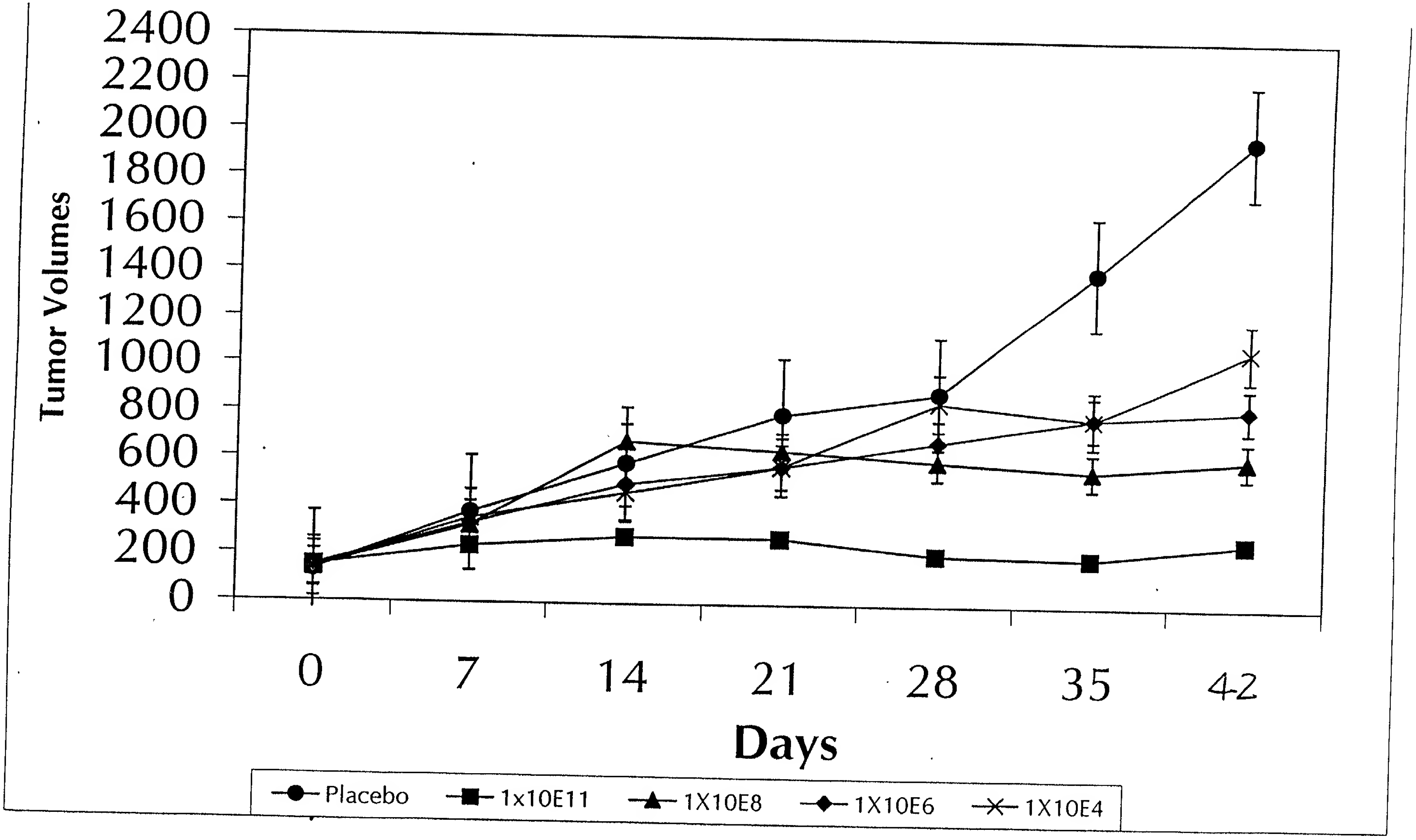

Tumor Volumes
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
7
14
21
28
35
42
Days
Placebo
1x10E11
1X10E8
1X10E6
1X10E4

FIGURE 26